

Psychopharmacology in Cancer

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Abstract Depression, anxiety, delirium, and other psychiatric symptoms are highly prevalent in the cancer setting, and pharmacological intervention is an important component in the overall psychosocial care of the patient. Psychopharmacology is also used as a primary or adjuvant treatment for the management of cancer-related symptoms stemming from the disease itself and/or its treatment, including sleep disturbance, loss of appetite, neuropathic pain, nausea, fatigue, and hot flashes. Psychiatrists, oncologists, and palliative care physicians working as members of a multidisciplinary team have the opportunity to target multiple symptoms that negatively affect a patient's quality of life with the strategic use of psychotropic medications when deemed appropriate. This article aims to review the indications for use of antidepressants, psychostimulants, anxiolytics, antipsychotics, and mood stabilizers in oncology. An updated review of the relevant literature is discussed and referenced in each section.

Keywords Cancer · Psychopharmacology · Depression · Anxiety · Cancer-related symptoms · Psycho-oncology

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Introduction

It is expected for a cancer patient to experience at least some level of emotional distress, but often this distress occurs with intensity and duration that becomes clinically relevant on multiple levels, negatively affecting quality of life, functional level, health behaviors, and cancer treatment adherence. Depressive and anxiety symptoms occur in approximately 25–40 % of cancer patients, although these estimates are lower when formal diagnostic criteria for psychiatric disorders are employed [1, 2]. When including other psychiatric disturbances that may present in the cancer setting such as delirium or other cognitive disorders, sleep disorders, and mania or psychosis due to medications or other medical conditions, the significance of addressing mental health issues in oncology becomes quite apparent. Hence, the National Comprehensive Care Network has established guidelines for the integration of psychosocial care in the cancer setting [3].

With international implementation of routine distress screening in the primary oncology setting, patients in need of psychiatric care are increasingly being identified. Intervention requires a multidisciplinary approach with involvement of oncology professionals, palliative care clinicians, social workers, nurses, psychologists, chaplains, psychiatrists, and others. The focus of this article is on psychopharmacology, a treatment approach utilized by prescribing clinicians in oncology, palliative care, and psychiatry. It is important to acknowledge that this is only one component of the comprehensive psychosocial care of the cancer patient, along with psychotherapy, integrative medicine, and other treatments.

Determining when to consider pharmacotherapy for symptom management can be challenging. Many of the Diagnostic and Statistical Manual (DSM) criteria for mental disorders overlap with cancer symptoms, particularly the neurovegetative symptoms of major depressive disorder [4]. Patient preference, availability of other approaches like

psychotherapy, past personal or family psychiatric history, economic and sociocultural factors, severity and need for rapid control of symptoms, and safety issues must be considered. Physiological and medical etiology of symptoms may point to pharmacotherapy as first-line treatment, such as endocrine therapies, steroid use, brain tumors, and infections. Inflammation due to cancer and its treatment may precipitate a variety of cancer-related symptoms with depression occurring in a “symptom cluster” along with fatigue, pain, anorexia, sleep disturbance, and cognitive dysfunction [5]. Psychiatric medications may be used to target these symptoms as well as other cancer-related symptoms including hot flashes, nausea, dyspnea, and hiccups [6].

Clinical trials examining the efficacy of psychiatric medication in cancer patients are limited, so prescribing strategies are extrapolated from studies conducted in otherwise healthy general psychiatric populations. Nevertheless, prescriptions for antidepressants, anxiolytics, and antipsychotics are provided frequently by both oncology and psychiatry clinicians, particularly when compared to healthy controls [7, 8]. Therefore, reviews on psychopharmacological interventions in cancer require updates to provide clinicians a reference to the newest findings in the medical literature and to address recent questions and controversies in the field [9, 10]. The purpose of this article is to review and update the clinician on the use of antidepressants, stimulants, anxiolytics, antipsychotics, and mood stabilizers for the management of both psychiatric and cancer-related symptoms.

Antidepressants

The clinician's first responsibility is to assess the nature of the emotional distress that may represent demoralization, social problems, or pain states treated more appropriately with interventions such as psychotherapy (cognitive-behavioral or other forms), problem-solving-focused counseling, or pain evaluation and management [11–13]. One study showed that sertraline neither improved symptoms nor survival in advanced cancer patients who did not suffer from major depression, supporting the idea that pharmacological efficacy is related to the presence of clinically significant depressive symptoms [14]. The use of both patient and clinician-rated scales, in addition to the clinical interview, is helpful to establish the diagnosis. These scales may also be utilized to more objectively track the results of treatment.

Depression and Anxiety

If the clinician decides to use an antidepressant, the selective serotonin reuptake inhibitors (SSRIs) remain the first drug

class of choice. They are relatively simple to dose with potential benefit/side effect ratios that tend to be higher compared to other classes of antidepressants. Also, there is now increasing interest in the possibility of inflammation as at least a cofactor in, if not etiologic to, the genesis of signs and symptoms of depression [15]. Inflammatory mechanisms may explain the increased prevalence of depression in physically ill people [16]. SSRIs have been found to have anti-inflammatory properties on microglia, the principal cells within the CNS that regulate and respond to inflammatory factors [17]. Because inflammatory mechanisms are implicated in cancer biology and physiology, SSRIs are, therefore, the more rational first option in managing depression associated with cancer. SSRIs may improve cancer patient immunity and have antitumor properties including *in vitro* apoptotic properties in hepatocellular carcinoma cells [18]. The corresponding clinical significance of these immunological and cellular effects requires further research.

The efficacy of antidepressants in cancer has been established in randomized, controlled studies [19–22]. In palliative interventions among patients with advanced cancers, SSRIs have also been found useful. Positive antidepressant response is associated with a certain genetic polymorphism of the serotonin transporter, an interesting factor that may explain a part of the reason why some patients do better with SSRIs and others do not [23]. One study suggests that in some patients with head and neck cancer, depression may be prevented by the use of escitalopram [24]. In a critical review of the literature, Callari et al. concluded that no SSRI is superior in depression associated with breast cancer [25]. In summary, all of these studies support the choice of an SSRI as an initial treatment option.

Cancer-Related Symptoms

It is a common clinical practice to utilize side effects or secondary clinical effects of antidepressants to the patient's advantage, particularly when other cancer-related symptoms present themselves alongside depression. Mirtazapine targets not only depression and anxiety but also insomnia, nausea, and anorexia [26]. Bupropion can be helpful for depression co-occurring with fatigue, poor concentration, or nicotine dependence, although tolerability in anxious patients may be problematic [27]. Neuropathic pain may respond to adjuvant treatment with venlafaxine, duloxetine, low-dose tricyclic antidepressants, and SSRIs [28, 29]. Two recent trials demonstrated the efficacy of venlafaxine in the prevention and relief of cancer pain syndromes, an intriguing new avenue of research [30, 31]. Venlafaxine and SSRIs are used to alleviate hot flashes stemming from hormone therapies, and trazodone is an efficacious non-habit-forming option for patients with insomnia [32].

Side Effects and Precautions

Other relevant issues associated with antidepressant use in cancer include side effects and drug interactions [33]. Medications commonly prescribed to cancer patients, such as tramadol, procarbazine, and linezolid, increase the risk of serotonin syndrome when serotonergic antidepressants are added. These agents also may exacerbate nausea and GI distress, and they may compound the risk of bleeding in patients with thrombocytopenia or on anticoagulants. Hyponatremia, discontinuation syndrome, and lowering of seizure threshold may occur. Cumulative anticholinergic, antiadrenergic, and cardiac toxicities limit the use of tricyclic antidepressants.

Tamoxifen is a selective estrogen receptor modulator used to prevent recurrence in patients with hormone receptor-positive breast cancer. The enzyme cytochrome 2D6 (CYP2D6) is the principal enzyme converting tamoxifen to its active metabolite endoxifen. Genetic variations in CYP2D6 affect the conversion of tamoxifen into its active form; about 7 % of women have nonfunctional CYP2D6 alleles and will have lower endoxifen levels. Four antidepressants—paroxetine, fluoxetine, duloxetine, and bupropion—are strong inhibitors of CYP2D6; they can interfere with tamoxifen metabolism [34]. The clinical relevance of this drug interaction has been controversial. A retrospective study showed a higher risk of death from breast cancer occurring among those who were on tamoxifen-paroxetine combined treatment, a report that changed the antidepressant prescribing practices of many providers [35]. Subsequent large studies examining the effect of various CYP2D6 metabolism phenotypes revealed no association with disease control and recurrence [36, 37]. Current clinical recommendations are to avoid strong inhibitors of CYP2D6 with preference for those with no or weak inhibition, but the clinician must be attuned to further studies on the issue as they become available [38]. Of note is that endoxifen is presently undergoing clinical trials in humans; in the future when it becomes clinically available, its use instead of tamoxifen may obviate much of the precaution against certain antidepressants [39].

Psychostimulants

Fatigue, experienced as low energy, mental slowing, or amotivation, is a ubiquitously reported symptom that negatively affects the quality of life of cancer patients [40]. Psychostimulants may be used to target these symptoms. They have a rapid effect on mood unlike antidepressants that require 2–6 weeks for response, and this can be a significant advantage when addressing depression in the palliative care setting [41]. In addition, cancer patients report improvement in energy, concentration, and overall sense of well-being. Stimulants

tend to improve appetite in the anorexic cancer patient, unlike in the general population. In the inpatient setting, this class of medication can provide a useful approach for the classic “failure to thrive” patient who has a decline in oral intake, communication, and participation in treatment or self-care [42]. If long-term management of depression is needed, stimulants can be used in short term until an antidepressant becomes effective. If narcotic pain medications are causing excessive sedation, stimulants can be added to the regimen to improve the patient’s ability to function throughout the day [43]. One small study pointed to efficacy in the management of hypoactive delirium [44].

Methylphenidate has been the most extensively studied psychostimulant in cancer populations [45]. A Cochrane review in 2010 indicated a slight improvement in cancer-related fatigue with methylphenidate, with subsequent studies mixed [46–48]. One large study found that long-acting methylphenidate is only beneficial in the subset of patients with more advanced cancer or severe fatigue [49]. The recommended initial dose is 2.5–5 mg orally twice a day in the morning and early afternoon. Both methylphenidate and dextroamphetamine are well tolerated, but potential side effects include agitation, anxiety, insomnia, xerostomia, appetite suppression, tremor, palpitations, rebound fatigue, and mood disturbance between doses. Cardiovascular effects involve elevation of blood pressure and heart rate, which should be monitored with each dose titration. Stimulants are contraindicated in cases of uncontrolled hypertension, unstable coronary heart disease, and arrhythmia. Electrocardiogram is recommended at baseline and after commencing the stimulant in patients with cardiac risk factors.

Modafinil and armodafinil affect histamine projections to the hypothalamus, differing from the sympathomimetic properties of methylphenidate and dextroamphetamine. There is less concern for abuse potential and cardiac safety with these drugs, but cytochrome P450 (CYP450) drug interactions must be identified when prescribing. Again data is mixed regarding the efficacy of modafinil in cancer-related fatigue, with benefit seen mainly in those patients with higher levels of baseline fatigue [50, 51]. Overall, although systematic data is limited, the clinician working with cancer patients is likely to find psychostimulants helpful in the management of depression and cancer-related symptoms in select patients.

Antipsychotics

In the oncology setting, antipsychotics are utilized in the management of conditions beyond primary psychotic and mood disorders, including delirium, psychosis due to another medical condition, and medication-induced psychotic disorder. In many cases, the side effect profile of select antipsychotics is harnessed to control target symptoms, as in the case

of anxiety symptoms, nausea, hiccups, loss of appetite, and insomnia.

Delirium

While underlying medical causes of delirium are addressed, antipsychotics play a key role in the management of agitation, sleep-wake cycle disturbance, and hallucinations. In addition, they may hasten stabilization and return of cognitive function [52]. Since there is no data suggesting overall superiority of any one particular antipsychotic, selection of an agent depends on the type of delirium (hyperactive, hypoactive, or mixed), route of administration, and potential toxicities in the context of the patient's medical comorbidities, age, and other medications [53]. For example, haloperidol remains the gold standard in managing delirious patients requiring intravenous (IV) administration, while aripiprazole may uniquely be activating in the case of hypoactive delirium [54, 55]. Intravenous chlorpromazine is helpful for agitated, combative patients with delirium.

Studies have demonstrated the efficacy of several atypical antipsychotics in the management of cancer-related delirium [56•]. Table 1 summarizes antipsychotics with at least one published clinical trial suggesting efficacy in the management of delirium in the cancer setting and clinical pearls about each agent. The newest antipsychotic agents, such as asenapine, iloperidone, lurasidone, and paliperidone, lack trial data in cancer. One small open-label trial suggests the efficacy of paliperidone in a general medical setting, as does a case series of lurasidone in ICU patients with prolonged corrected QT interval (QTc) [57, 58].

A relatively new and important area of research involves the prevention of delirium in high-risk populations. A meta-analysis of five recent studies revealed a 50 % relative risk reduction in delirium occurrence postoperatively in elderly patients administered prophylactic antipsychotics [59•]. Studies of prophylactic antipsychotic use in select cancer populations at points in the treatment trajectory associated with an elevated risk of delirium are needed.

Anxiety, Depression, and Insomnia

For acute anxiety in the cancer setting, antipsychotics may be preferable to benzodiazepines since the latter increases the risk of altered mental status and respiratory depression. For similar reasons, low doses of sedating atypical antipsychotics such as quetiapine and olanzapine are used to address insomnia when other sedative-hypnotics are deemed too risky [60, 61]. Data from studies in psychiatric, non-cancer patients point to several atypical antipsychotics as useful augmentation strategies in anxiety and depressive disorders [62, 63]. Although there are no empirical, cross-validation studies in oncology populations,

Table 1 Antipsychotic medications for treatment of delirium in the cancer setting

Medication	Route of administration	Clinical pearls
Haloperidol	PO, IV, IM, OS	IV administration poses less risk for EPS than PO Antiemetic properties IV/IM dose 2× as potent as PO IV administration poses a high risk of QTc prolongation
Chlorpromazine	PO, IV, IM, OS, PR	Unique PR administration Highest risk of orthostatic hypotension Most sedating IV/IM 2–4× as potent as PO
Risperidone	PO, OS, ODT	EPS risk at high doses Highest risk of prolactin elevation
Olanzapine	PO, IM, ODT	Antiemetic properties Appetite stimulating and sedating
Quetiapine	PO	Low risk of prolactin elevation Appetite stimulating and sedating
Ziprasidone	PO, IM	Less sedating Low risk of metabolic side effects High risk of QTc prolongation Low risk of prolactin elevation
Aripiprazole	PO, IM, ODT, OS	May be stimulating Low risk of metabolic side effects Least QTc prolongation May lower prolactin levels

Consider the risks and benefits of the use of antipsychotics carefully when treating older adults, especially those with underlying cognitive and cardiac problems due to reports of increased mortality and increased risk of cardiovascular and cerebrovascular events among older adults with dementia treated with antipsychotics

PO oral, IV intravenous, IM intramuscular, ODT oral disintegrating tablet, PR per rectum, OS oral solution, EPS extrapyramidal symptoms

experience suggests that these findings may be extrapolated to cancer patients with high levels of anxiety or depression throughout the treatment course who are refractory to monotherapy with serotonergic antidepressants.

Nausea, Hiccups, and Appetite

Nausea, whether chronic or opioid-induced, has long been treated with haloperidol in the palliative setting, although the data regarding efficacy is controversial [64]. The treatment algorithm for intractable hiccups includes both haloperidol and chlorpromazine, although they are not first line [65]. Olanzapine has shown efficacy in the treatment of chemotherapy-induced nausea and vomiting [66]. Although quetiapine and olanzapine can be troublesome in general psychiatry due to side effects of increased appetite and weight gain, these properties can be helpful in addressing cancer-related anorexia [67].

Side Effects and Precautions

Cancer patients may be at greater risk for adverse events because of their compromised medical status. For instance, volume depletion may heighten risk for orthostatic hypotension resulting in syncope and falls. Intramuscular (IM) route of administration of antipsychotics is associated with risk for hematoma in cancer patients with thrombocytopenia. Although a comprehensive review of all potential side effects is beyond the scope of this review article, key concerns in the cancer setting are described in more detail below.

The issue of antipsychotic-induced hyperprolactinemia in breast cancer patients is of increasing concern given that the majority of intraductal tumors overexpress the prolactin receptor and that prolactin may promote tumor progression regardless of receptor status. Of the antipsychotics most commonly used in the cancer setting, risperidone and haloperidol are most likely to cause hyperprolactinemia, while aripiprazole, ziprasidone, and quetiapine cause minimal elevation [68•].

Akathisia, a troubling subjective sense of restlessness, may develop along with other extrapyramidal symptoms (EPS), especially when antipsychotics are combined with antiemetics. This distressing side effect can be rapidly addressed with administration of clonazepam, propranolol, diphenhydramine, or benztropine if needed.

Regular monitoring of QTc on electrocardiograph (EKG) is important, particularly in cancer patients with electrolyte abnormalities and those on other QTc-prolonging medications, since QTc prolongation may predispose to torsades de pointes. Intravenous haloperidol and ziprasidone have the highest risk of QTc prolongation. A recent meta-analysis of antipsychotics in schizophrenia noted that the least QTc-prolonging antipsychotics are aripiprazole, lurasidone, paliperidone, and asenapine [69].

Additional concerns when prescribing antipsychotics include the risk of metabolic syndrome with long-term use (i.e., insulin resistance, dyslipidemia, obesity), hyponatremia, decreased seizure threshold relevant in the context of steroids and brain tumor, drug interactions, elevation of liver transaminases, and anticholinergic toxicity (e.g., constipation, dry mouth, urinary retention).

Anxiolytics and Hypnotics

Cancer patients may develop anxiety acutely under the stress of illness or as an exacerbation of a preexisting anxiety disorder [70–72]. Pharmacological treatment for cancer-related anxiety aims to reduce emotional distress that may impair functioning, treatment adherence, ability to make treatment

decisions, and inadvertently increase length of hospital stays [73].

Anxiety

Although serotonergic antidepressants remain to be the primary approach to pharmacological management of generalized anxiety and prevention of panic attacks in cancer patients, treatment also often includes short and long-acting benzodiazepines (BDZs) and non-benzodiazepine medications (see Table 2). BDZs are well-tolerated, safe, and effective drugs for short-term use; their anterograde amnesic properties have been found to lessen the negative impact of cancer treatment experiences. Shorter-acting benzodiazepines may be sufficient for procedure-related and anticipatory anxiety or specific phobias (e.g., needles, closed MRI). Longer-acting anxiolytics, such as clonazepam, may help with the unpredictable timing of hospital routines and decrease the potential for rebound anxiety or end-of-dose failure from short-term benzodiazepines.

As discussed in corresponding sections of this review, sedating antipsychotics are effective in controlling anxiety refractory to therapeutic doses of benzodiazepines or for those patients with respiratory compromise. Gabapentin, an antiepileptic drug, has been a successful alternative treatment for anxiety in breast cancer survivors [74]. Beta-blockers also show promise in reducing intrusive thoughts after new cancer diagnoses [75•]. The serotonergic agonist buspirone may be helpful for generalized anxiety symptoms. Hydroxyzine is an antihistamine that may be administered as needed for anxiety symptoms. A key advantage of these non-BZD medications is that they are not generally associated with tolerance, abuse, or dependence.

Insomnia

Benzodiazepines, such as lorazepam, temazepam, and clonazepam, are frequently prescribed to help people sleep when going through acute crises. Long-term use can cause tolerance and loss of efficacy. Zolpidem, eszopiclone, and zaleplon, also known as “Z drugs,” are non-benzodiazepine hypnotics with minimal anxiolytic effect and lower risk for tolerance and dependence, but amnesia, and rarely hallucinations, has been reported [10•, 76, 77]. In the cancer setting, non-benzodiazepine hypnotics have been shown to be efficacious and safe, even when combined with other psychotropics [78–80]. Sedating antidepressants, such as mirtazapine, trazodone, amitriptyline, and doxepin, low-dose sedating atypical antipsychotics, antihistamines, and melatonin agents can all be used to manage insomnia as well [81].

Table 2 Medications commonly prescribed for anxiety and insomnia in cancer

Medication	Daily/as needed dosing	Remarks
Benzodiazepines^a		
Alprazolam	0.125–1 mg two to four times daily or as needed Extended release formulation for daily dosing	Shorter acting May cause rebound anxiety Rapid onset good for panic symptoms Difficult to taper Higher addictive risk Oral disintegrating tablet available
Lorazepam	0.5–1 mg two to three times daily or as needed	Available in IV form Intermediate acting May help with chemotherapy-related nausea Preferred if hepatic insufficiency
Clonazepam	0.125 mg–1 mg two to three times daily or as needed	Longer acting Orally disintegrating tablet available Useful in preventing panic symptoms and generalized anxiety
Diazepam	2–10 mg two to three times daily or as needed	Available in an IV form Longer acting Rapid onset; good for panic symptoms Higher addictive risk
Temazepam	7.5–30 mg at bedtime as needed	Used for insomnia, not anxiety Preferred benzodiazepine if hepatic insufficiency
Non-benzodiazepines for anxiety		
Buspirone	5–15 mg two to three times daily ATC for anxiety	Can take several weeks to see anxiolytic effect; well tolerated; no withdrawal
Non-benzodiazepines for sleep		
Z drugs		
Zolpidem	5–10 mg bedtime as needed or 6.25–12.5 mg CR	For insomnia Less tolerance and addiction than benzodiazepines May cause amnesia, falls, disorientation, and hallucinations
(es)Zopiclone	1–3 mg bedtime as needed	May cause metallic taste
Zaleplon	5–10 mg bedtime as needed (max 20 mg as needed)	
Rozerem	8 mg bedtime as needed	Works on melatonin system (agonist) May take longer to take effect

ATC around the clock, CR controlled release

^aUsed for anxiety and insomnia and may cause sedation, falls, confusion, and respiratory depression in cancer patients. Smaller daily doses can be considered in older, frail adults to avoid side effects

Cancer-Related Symptoms

Benzodiazepines, in combination with antiemetics, relieve chemotherapy-induced nausea and vomiting. Lorazepam can be given intravenously for fast action or when oral intake is problematic. Both alprazolam and clonazepam come in dissolvable tablets when swallowing pills is difficult. Short-acting BDZs like midazolam are used in the palliative setting to address other symptoms beyond anxiety and pain, such as pain, dyspnea, restlessness, and agitated delirium [10•].

Side Effects

The most common side effects of BZDs include sedation, dizziness, falls, respiratory depression, motor

incoordination, and confusion, especially in elderly patients and when combined with other CNS-depressant medications like narcotic pain medications. Patients with central nervous system disease are at greater risk for paradoxical effects of BZDs with heightened anxiety, agitation, and disinhibition [9, 82].

As with most psychotropics, BZDs are metabolized by the CYP450 system that may lead to drug interactions. Although still a concern, the development of BZD dependence in patients without prior history of substance dependence is relatively uncommon as cancer patients generally do not take more medication than they absolutely require and discontinue medications as their anxiety remits. Nevertheless, long-term use of these agents should be monitored carefully and further study is warranted [83•].

Mood Stabilizers

The three major classes of mood stabilizers for the treatment of bipolar disorder are lithium, antiepileptic drugs (AEDs), and atypical antipsychotics [84]. In the cancer setting, mood stabilizers are prescribed for the management of other indications including irritability, impulsivity, and temper dyscontrol associated with steroids, brain tumors, or other medical conditions; they may also treat neuropathic pain and hot flashes and provide seizure prophylaxis [32, 85, 86].

Lithium is seldom started in the cancer context due to risk of dehydration, electrolyte abnormalities, renal dysfunction, and drug interactions that may result in toxicity. Of interest, it has been suggested in the literature that lithium be used for post-chemotherapy prolonged neutropenia or in stem cell mobilization and engraftment after stem cell transplant due to its granulocyte-stimulating properties [87]. Others have suggested its use as a neuroprotective agent to prevent chemotherapy-induced cognitive dysfunction [88].

Valproic acid (VPA) can be helpful in cases of mood lability, impulsivity, and disinhibition, whether these symptoms are due to primary psychiatric or other medical causes [89]. Levetiracetam is commonly prescribed for seizure prophylaxis in brain tumor patients, but it is associated with depression and irritability [90]. Switching to another anticonvulsant like VPA may be beneficial in such cases. One study found a survival benefit in glioblastoma patients taking VPA versus no or other anticonvulsants, suggesting potential antitumor properties [91]. Carbamazepine is an adjuvant analgesic with a specific indication in trigeminal neuralgia. Both VPA and carbamazepine carry the risk of several adverse effects including hematological suppression and hepatotoxicity, significant concerns in patients on chemotherapy or with hepatic tumors. Drug interactions and serum levels of these medications must be monitored as carbamazepine is a hepatic CYP450 enzyme inducer and VPA an inhibitor [92].

Gabapentin and pregabalin are used to manage hot flashes due to hormonal treatments and neuropathic pain, with specific indications for postherpetic neuralgia [93–96]. Small trials have shown the efficacy of gabapentin for pruritus and chronic noninfectious cough [97, 98]. Anxiolytic and sedative effects of these drugs can be harnessed to target multiple cancer-related symptoms [74, 99]. A key advantage of these AEDs is renal clearance with no CYP450 drug interactions; use should be avoided in severe renal insufficiency. Pregabalin should be avoided in patients with congestive heart failure. Ataxia, dizziness, and peripheral edema may occur, and both agents should be tapered after prolonged use to prevent withdrawal symptoms and seizure.

Lamotrigine, an AED used in bipolar depression, has mixed data regarding efficacy in neuropathic pain [100]. It is commonly associated with a skin rash that, in rare cases, can progress to life-threatening Stevens-Johnson syndrome. Nonpsychiatric applications of topiramate beyond seizure prophylaxis include migraine, essential tremor, and neuropathic pain [101]. In cancer patients with binge-eating disorder or obesity, a risk factor for worse cancer outcomes, this AED may play a role [102]. Cognitive disturbance, nephrolithiasis, metabolic acidosis, and decreased efficacy of oral contraceptives are important adverse effects to keep in mind. Finally, a recent open-label study of oxcarbazepine in colon cancer patients demonstrated efficacy in the prevention of oxaliplatin-induced neuropathy, pointing to a promising new avenue for future research and potential clinical application of AEDs [103].

Conclusions

In summary, the identification of oncology patients in need of intervention for depression and anxiety in the context of co-occurring cancer-related symptoms is rapidly improving due to dissemination of distress screening practices. Empirical data regarding the use of psychopharmacological agents in the cancer setting is limited, and future trials in the treatment and even prevention of symptoms in high-risk patients are indicated. Clinical databases, despite generating uncontrolled data, will help to supplement our collective experience in prescribing in cancer populations. Psychiatric professionals with expertise in this area are charged with educating front-line oncology colleagues because patients frequently cannot or will not see a mental health professional during their cancer treatment. Monitoring for drug interactions between prescription drugs and over-the-counter or herbal remedies is essential, and electronic drug interaction programs and tools are invaluable for this purpose. Due to the medical vulnerability of this population, cautious and judicious prescribing practices are advised. All clinicians who are part of a multidisciplinary team addressing the psychosocial needs of cancer patients should stay abreast of developments as they emerge.

Compliance with Ethics Guidelines

Conflict of Interest Seema M. Thekdi, Antolin Trinidad, and Andrew Roth declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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